## INTRODUCTION AND OVERVIEW

### A. SPECIFIC AIMS

This proposal specifically addresses "Cancer Screening and Management", one of the six focus areas identified by the DHHS in which racial and ethnic minorities experience serious disparities in health access and outcomes. This CPHHD is motivated by the following observations:

- There are significant gaps in our knowledge of the factors that predict prostate cancer outcomes, and about the reasons for disparity in prostate cancer-related health outcomes between African American and Caucasian men. The proposed research seeks to fill these gaps.
- Advances in molecular genetics provide an unprecedented opportunity for learning about the biological influences on prostate cancer outcomes in the context of other behavioral, social, and demographic factors.
- The University of Pennsylvania has existing multidisciplinary research resources related to the study of prostate cancer outcomes, including studies of the genetics, quality of life, patterns of care and treatment decision making after the diagnosis of prostate cancer.
- There has been tremendous recent growth in transdisciplinary research addressing the biological, behavioral, and social determinants of health at the University of Pennsylvania. Penn has outstanding capacity to conduct innovative research through transdisciplinary collaboration across molecular biology, genetic epidemiology, sociology, economics, psychology, biomedical informatics, and health policy.
- The proposed research has implications for clinical and public health practice, with potential to catalyze critical improvements in the prevention and management of prostate cancer.

We proposed three specific aims in response to these observations:

***Specific Aim 1*: To conduct four highly interrelated research projects aimed at identifying factors that influence prostate cancer outcomes.** Specifically, these projects will evaluate the role of: (1) physician and patient factors in the use of prostate cancer screening (J. Holmes, PI), (2) prostate cancer screening and genes involved in hormone metabolism and immune surveillance on prostate cancer outcomes (T. Rebbeck, PI); (3) racial residential segregation on patterns of health care and outcomes for prostate cancer (K. Armstrong, PI), and (4) social, cultural, behavioral and environmental factors on quality of life after a prostate cancer diagnosis (C. Hughes, PI). The goals of these projects are to integrate knowledge about biological, behavioral, social environmental and physical environmental factors that contribute to disparities in the health of men diagnosed with prostate cancer.

***Specific Aim 2*: To create three specialized cores to serve the needs of these projects and the Center.** These include: (1) an Administrative Core to oversee and evaluate the CPHHD and to facilitate transdisciplinary collaboration; (2) a Community Outreach and Dissemination Core to advise all projects on the accrual of study participants, facilitate ongoing interactions with our community partners, and disseminate the information gained from this research to the public health community and general population; and (3) a Biomedical Informatics Core to provide integrated data management and model-building for the multivariate analysis of biological, behavioral, social, and environmental factors on prostate cancer outcomes.

***Specific Aim 3*: To solicit and support a series of focused developmental (pilot) research projects.** These projects will be chosen to extend the primary research projects to additional studies of cancer screening, biological interactions, statistical model building for the integration of complex data from various disciplines. Criteria for these and other pilot projects will be selected based on scientific merit and the potential for sustained external funding. The goal of these developmental projects is to expand the scope of the research proposed in the Projects described here and to enhance the multidisciplinary research team with members representing additional disciplines and expertise.

### B. SETTINGS AND FACILITIES

#### B.1 Abramson Cancer Center (ACC) at the University of Pennsylvania

The ACC is an NCI-designated comprehensive cancer center that was founded in 1973 and recently renamed to serve as the focus of cancer-related research, patient care, and educational activities at the University of Pennsylvania. John H. Glick, M.D., has served as the Center's Director for the past 12 years. The ACC provides an organizational framework that promotes and enhances interdisciplinary cancer research within the School of Medicine and throughout the University. Its mission is defined through seven primary objectives: develop and support cancer-focused Research Programs (basic, clinical, translational, and cancer control) that are interdisciplinary and interdepartmental in nature; develop and support interdepartmental educational and research training programs for physicians, scientists, students, nurses, and others; recruit and support new faculty with a commitment to cancer research; facilitate investigator collaboration within and among Research Programs; develop and manage Shared Resources; acquire and allocate laboratory space for active cancer researchers; and foster interdisciplinary patient care programs and activities. The ACC has

more than 330 physicians and scientists in 41 University Departments and 8 schools. Most Cancer Center members are from the School of Medicine, while others are from the Schools of Veterinary Medicine, Dental Medicine, Nursing, Social Work, Wharton Business, and Arts and Sciences. ACC members have over $63 million of extramural funding. Collaborative working relationships are well-established among ACC members from different Departments and Schools as is evidenced in all aspects of ACC research, patient care and educational activities. The ACC has provided substantial direct support to this CPHHD in terms of support for faculty salary, program development, and resource infrastructure (see description of institutional commitment).

**B.2. The Leonard Davis Institute (LDI)**

Since 1967, LDI has been the center of the University of Pennsylvania's activities and programs in health services research, health policy, and health care management executive education. as a formal cooperative venture among Penn's schools of medicine, business, nursing, and dental medicine, LDI represents one of the earliest efforts to promote collaborative scholarship in health care through formal partnerships within the same university among the clinical, management, and social sciences.. Through conferences, seminars, and publications, LDI translates the results of health services research into a form that is useful and accessible to public and private decision makers. LDI Senior Fellows include about 150 of the most distinguished scholars in health, management, economics, ethics and the social sciences. Last year, LDI Senior Fellows received approximately $30 million in research grants.

LDI has developed an innovative policy dissemination program that is used by many investigators at Penn to reach key audiences and analyze the policy implications of research results. LDI's Policy and Research Program (PreP) identifies opportunities for dissemination of results beyond academic journals and professional meetings, and tailors materials to targeted groups of policymakers in the community and public and private sector. LDI publishes monthly *Issue Briefs*, which are four-page summaries of research results that highlight their social and policy relevance. They are written in easy-to-understand language with bullet points, headers, margin cut-outs and other devices to enhance delivery of the message. They are professionally written, formatted, printed and distributed to an LDI mailing list of more than 4,000 researchers, clinicians, administrators, federal, state and local; legislators and officials, and industry and community leaders. For each *Issue Brief*, LDI works with investigators to identify key audiences that are not on the general mailing list. In addition to hard copy mailings, these *Issue Briefs* are also posted on relevant web sites to increase their reach and accessibility. PreP offers other materials and services as each project or center requires, such as downloadable slide presentations, consensus development conferences, or policy roundtables. This program is a central feature of the CPHHD.

**B.3. Center for Clinical Epidemiology and Biostatistics (CCEB)**

The CCEB was created in February 1993. Through its predecessor, the Clinical Epidemiology Unit (CEU), now subsumed within the CCEB, the CCEB has been involved actively in clinically oriented epidemiologic teaching and research since 1978. It is the primary home for epidemiology and biostatistics at the University of Pennsylvania. The CCEB has been directed by Brian L. Strom, M.D., M.P.H. since 1980 (then the CEU). The CCEB launched a major expansion in 1995 to create a Biostatistics Unit (BU) to match the depth and breadth of the CEU. The extension of the CCEB's biostatistics program led to the recruitment of J. Richard Landis, Ph.D., to provide senior leadership for the rapidly expanding BU. Dr. Landis joined the CCEB in 1997 and brought with him a Clinical Research Computing Unit (CRCU), designated as a core research facility providing "state of the art" services for clinical data management and research computing.

The CCEB is an interdisciplinary and interdepartmental program. Its mission is to improve the health of the public by linking epidemiology, biostatistics, and clinical medicine, bringing epidemiologic research methods to clinical research, clinical insight to epidemiologic research, and an understanding of research methodology to clinical medicine. CCEB activities focus on the performance of clinical epidemiologic research, biostatistical research and methodology development, the conduct of multicenter clinical trials, collaboration with biomedical and clinical researchers across diverse scientific disciplines, and curriculum development and teaching of clinical epidemiology and biostatistics at the undergraduate and post-graduate levels. The CCEB was awarded approximately $22 million in extramural grants in 2000-2001 alone, and counts among the top 5 U.S. programs in Biostatistics or Epidemiology in extramural funding.

**B.4. National Black Leadership Initiative on Cancer (NBLIC)**

We have an ongoing relationship with Philadelphia Chapter of the NBLIC, and will work together with this organization in the development and implementation of this CPHHD. The Philadelphia chapter of NBLIC was founded in 1992 as part the National Cancer Institute's program to establish a national system of community-based outreach for cancer prevention and control in the African American population. The overall objective of the NBLIC is to develop, implement, and support community-based programs for cancer prevention and control; specific activities of the Philadelphia chapter of the NBLIC include development of applied research projects and implementation of community outreach and education programs for cancer prevention and control. The NBLIC's goals are: 1) to reduce cancer incidence and mortality rates; 2) to improve cancer survival rates; and 3) to address the barriers that limit or

and mortality rates; 2) to improve cancer survival rates; and 3) to address the barriers that limit or prevent African Americans from gaining access to quality cancer control services. The Philadelphia chapter has been actively involved in cancer prevention and control initiatives in the African American community. Past work has included successful efforts that prevented targeted marketing of tobacco products to the African American community. Since 1999, the NBLIC's activities have been focused on reducing morbidity and mortality for breast, colon, and prostate cancer. Currently, the NBLIC members represent community organizations, public health officials, health care providers, and academic institutions.

Our partnership with the NBLIC began in 2001 with discussions about the complementary goals of the ACC, the Community and Minority Cancer Prevention and Control Initiative (CMCI), and the NBLIC to identify areas of mutually beneficial collaborations. This provided the foundation upon which the proposed collaboration for this CHHD is based (see Project 4 for detailed discussion of the developmental process). For example, through this partnership, the ACC and NBLIC have developed and implemented community information symposia related to breast cancer in African American women and participated in a church-based prostate cancer screening program. We are also working together to develop and implement cancer education programs through a community health referral network. While the partnership that is proposed for the CHHD is the first formal partnership for research, we believe that our prior work together in community education, extensive discussion about our respective objectives and missions, and past and ongoing dialogue about research priorities has provided a strong foundation for the proposed partnership and has placed us in an ideal position to ensure a successful and mutually beneficial collaboration through this CHHD.

**B.5. 50 Hoops**

50 Hoops is a non-profit organization with the goal of community outreach and dissemination of education on prostate cancer. 50 Hoops has hosted basketball tournaments for men over the age of 50, with a particular focus on the African American community. These tournaments have been held in cities throughout the United States, including Houston, Dallas, Washington D.C., Detroit, and Philadelphia. These tournaments provide educational opportunities for men at increased prostate cancer risk and their families, as well as an opportunity for free prostate cancer screenings. Through these tournaments and the accompanying publicity that has been generated from them, 50 Hoops raises awareness about prostate cancer risk and prevention. The 50 Hoops organization has also been successful in creating a process for identifying and contacting prostate cancer patients and families of all races to support research and clinical trials. The research data that arise from this CPHHD will be translated to the 50 Hoops events through educational materials and sessions. Dr. Rebbeck (PI of the CPHHD) serves on the 50 Hoops National Advisory Board.

**B.6. INSTITUTIONAL COMMITMENT AND RELATIONSHIP TO P30-FUNDED CANCER CENTER**

Drs. John Glick (Director of the ACC), Dr. Brian Strom, (Director of the CCEB), and Dr. David Asch (Executive Director of the LDI), are fully committed to the development of the proposed CPHHD (see attached letters of support). These units have a long-term track record in providing generous commitment and support for developing the resources and infrastructure needed to conducting leading edge research related to prostate cancer and health disparities. Among the CPHHD-related efforts supported by these units are: developmental funds for new research projects; recruitment and start-up funding of new faculty; salary support for faculty with leadership positions; provision of research space and laboratory facilities; funding and support of core facilities; facilitation of collaborative research initiatives across disciplines and departments; and sponsorship of research meetings, seminars and retreats.

Many of the investigators involved in this center grant, including Drs. Rebbeck, Hughes, Armstrong, and Holmes, have directly benefited from this commitment. The ACC has provided each of these investigators with recruitment and start-up funds, pilot project funding, partial salary support, research space, access to core facilities required for their particular type of research, and, perhaps most importantly, the ACC's full and consistent support in establishing a nationally recognized research effort in prostate cancer and health disparities. This support includes the following:

- Dr. Rebbeck is the leader of the ACC's Cancer Epidemiology Program, and receives salary support from the ACC and CCEB for his role as program leader. This support directly offsets a portion of the salary support for Dr. Rebbeck's participation in this CPHHD. The ACC and CCEB were actively involved in recruiting Dr. Rebbeck to Penn, and provided partial start-up funding support. Dr. Rebbeck has also received developmental funds for new pilot studies. The ACC provides support for seminars and retreats in the area of cancer epidemiology under Dr. Rebbeck's direction.
- Dr. Hughes is leader of the Community and Minority Cancer Prevention and Control Initiative of the Cancer Center. She receives support for both this initiative and her research program. The ACC has also provided and renovated office space for Dr. Hughes' research program which will be used by the proposed CPHHD. The ACC was actively involved in recruiting Dr. Hughes to Penn as part of its long-term commitment to establishing special expertise in the area of community and minority cancer prevention and control.
- Dr. Liebman is leader of the Biomedical Informatics Program for the ACC. He was recruited because of the ACC's commitment to creating a nationally recognized resource in biomedical informatics. Dr. Liebman receives full salary

support from the ACC, which also provides Dr. Liebman's research space, computational facilities, and salary support for his research staff. All of these will be used extensively by this CPHHD (see also Biomedical Informatics Core). The ACC has also allocated funds to support the Biomedical Informatics Program strategic plan, which will be completed in the coming years.

- Dr. Holmes is a member of the Biostatistics Unit in the ACC. The ACC was actively involved in recruiting Dr. Holmes using ACC funds. Dr. Holmes currently receives 5% salary support for his work from the ACC.
- Dr. Schwartz has led the Health Services Program of the ACC and LDI for many years, and receives a portion of his salary from these units. This support directly offsets a portion of his salary support for this CPHHD participation.
- Dr. Armstrong has received support from the ACC and CCEB for pilot research related to mammography screening among low-income women.

In addition to these individual levels of support, all investigators have access to the substantial ACC core resources. These include use of the Biostatistics facility, the Biomedical Informatics resource led by Dr. Liebman, and core facilities including a genoptying core laboratory. Many of these core facilities will be used directly to support the research of this CPHHD application. The ACC provides $5,000 per year in support of seminar speakers on topics related to this CPHHD. These funds will be used to bring in speakers from outside the University and to defray local costs. The use of these funds is described in detail in the Administration Core. The CCEB will provide appropriate offices in contiguous space for the activities of the Administrative Core to maximize communication among the investigators and staff.

## C. PROPOSED USE OF HUMAN SUBJECTS

The proposed research projects involve human subjects. The CPHHD will work closely with two bodies that oversee research at the University of Pennsylvania. First, the Committee for Research Involving Human Beings (the local Institutional Review Board) reviews and approves all research involving human subjects at the University of Pennsylvania. In addition, the Clinical Trials Scientific Review & Monitoring Committee of the ACC provides an additional level of oversight into cancer-related protocols, including all four projects of this CPHHD, and will oversee bioethical aspects of the development and execution of the proposed research.

*Demographics of Study Participants***.** Because the focus of this CPHHD is prostate cancer, all study participants will be men. However, focus groups and community outreach activities (e.g., 50 Hoops, NBLIC) will include women. The CPHHD will focus on the Philadelphia metropolitan area, with each project providing complementary insights into the Philadelphia community. Projects 1, 2 and 4 will draw study participants directly from the Philadelphia metropolitan area, with a particular focus on the West Philadelphia community. Project 3 will use national Medicare data to examine the effect of characteristics of the metropolitan area on outcomes, thereby elucidating their contribution to racial disparities in Philadelphia. The primary ethnic groups in Philadelphia are African American (28% of the total population) and Caucasian (67% of the total population). Based on prior experience and on Pennsylvania Tumor Registry statistics, we anticipate that less than 5% of men ascertained from Philadelphia will be of other ethnicities. Therefore, the statistically most meaningful analyses will involve African American and Caucasian men. However, men of all ethnicities will be ascertained and studied in the research conducted in this CPHHD. Additional details about study populations, women and minorities, and human subject issues can be found in each of the research project applications.

*Privacy Protection***.** Protection of privacy of participants in studies involving biosamples and genetic information is of the utmost importance, and we have extensive experience in this area. First, all information will be housed on a secure and password protected server maintained by the Biomedical Informatics Core. Only study personnel at the University of Pennsylvania will have access to these research databases. Materials that are shared with community groups or other dissemination activities will only be reported in aggregate, and will never include information that identifies individuals as participants in a research study. Second, any communications made by e-mail will use unique, unlinked ID numbers only and never include names or other personal information. Third, because the biomarkers to be studied in this research have no established clinical significance, individual laboratory-based genotype results will never be communicated to research participants, and no identifying information will be linked to biomarker data during analysis. Fourth, all data will be kept in locked files accessible only by the study PI and a limited number of study staff. Fifth, biosamples will be sent to the laboratory labeled only with a non-identifying code. The laboratory will never have access to identifying information. Information about genotype will never be included in any medical records. Sixth, we will obtain a federal Certificate of Confidentiality to further protect confidentiality of study participants. Seventh, in all data sets, including those with laboratory results, we will use ID numbers only. A separate data set linking names with ID numbers will be accessible only by the Project PI or senior programmer.

E.

## D. ORGANIZATION OF THE CENTER

### D.1. Center Oversight and Structure

**D.1.a.** ***Administrative Core***. This core will be led by the CPHHD Principal Investigator (Dr. Rebbeck) and Co-Principal Investigator (Dr. Hughes). This core will be responsible for the overall management of the CPHHD which is

executed through the Executive Committee (twice a year), Steering Committee (once per month), and External Advisory Committee (once a year). The Administrative Core will also serve other CPHHD functions, such as communication within and beyond the CPHHD and outreach (see Administrative Core proposal).

**D.1.b. *Executive Committee***. This committee will include the CPHHD PI and Co-PI, Project PIs, Core Directors, the Director of the Urologic Oncology Program, and the Director of the ACC. This body will meet twice a year. This group will formulate CPHHD policy, identify and respond to special research opportunities and challenges, and manage the CPHHD budget.

**D.1.c. *Steering Committee***. This committee will include all of the members of the Executive Committee, as well as the project co-PIs and core directors. This committee will meet monthly. In contrast to the Executive Committee, the Steering Committee will oversee day-to-day management of the components of the CPHHD. The Steering Committee will review project participant accrual, data collection, analysis and report preparation; core usage and satisfactory progress toward achieving the goals of the Center; and success of strategies to foster transdisciplinary collaboration.

**D.1.d. *External Advisory Committee.*** This committee will be comprised of advisors from outside the University of Pennsylvania representing the broad range of disciplines in the CPHHD, including psychology, behavioral sciences, genetics, epidemiology, clinical sciences (e.g., medical oncology, urology), and health policy. This committee will also include members representing community-based or consumer organizations. This group will be convened annually to review the progress in each of the CPHHD components to identify new scientific opportunities, and to engage in strategic planning with the CPHHD leadership. Selected members of the External Advisory Committee will also be invited for a mid-year consulting visit and to present at the ACC Grand Rounds.

**D.2. CENTER LEADERSHIP**

The PI of the overall CPHHD is Dr. Timothy Rebbeck. He will provide direction and oversight to the entire program, and lend particular expertise for the epidemiology and genetics aspects of the CPHHD's research program. Dr. Chanita Hughes is co-PI of the CPHHD. She is Director of the Community and Minority Cancer Prevention and Control Initiative of the ACC, and will provide oversight and direction for the behavioral, environmental, and social aspects of the CPHHD's research program.

**Timothy R. Rebbeck, Ph.D.** is Associate Professor of Epidemiology in the Department of Biostatistics and Epidemiology, a Senior Scholar and Director of the Human Genetics Program in the CCEB, and Leader of the ACC's Cancer Epidemiology Program. The goal of Dr. Rebbeck's research program is to understand the complex, multifactorial etiology of cancer. This research uses a multidisciplinary approach that combines methods from epidemiology, statistics, molecular biology, and classical genetics. Dr. Rebbeck directs The Laboratory for Molecular Epidemiology that is geared toward the generation of molecular biomarker data for family and epidemiological studies. Dr. Rebbeck also has significant research interest and experience in studies of prostate cancer etiology. He holds an NIH grant entitled "Molecular Epidemiology of Prostate Cancer (R01-CA85074), which is an ongoing, large-scale epidemiological study to evaluate risk factors for prostate cancer, with a focus on genetic markers of etiology in African American and Caucasian men in Philadelphia. Dr. Rebbeck has had several leadership and collaborative roles in transdisciplinary group projects such as that proposed here. Dr. Rebbeck has been an active collaborator with the Cancer Genetics Network, and the University of Pennsylvania/Wistar Institute SPOREs (Specialized Programs of Research Excellence) on leukemia and cancers of the skin. Dr. Rebbeck is PI of a large, multicenter study involving 14 institutions in North American and Europe entitled "Prophylactic Surgery in Carriers of BRCA1 and BRCA2 Mutations" (R01-CA83855). Dr. Rebbeck is also currently co-PI and co-Director of the Administrative Core for a Program Project entitled "Molecular Susceptibility to Hormone-Induced Cancer" (P01-CA77596), which will expire in the Summer of 2003. These projects have provided Dr. Rebbeck with substantial direct experience in leading a large-scale, transdisciplinary research project such as that proposed here.

**Chanita Hughes, Ph.D.,** is an Assistant Professor in the Department of Psychiatry at the University of Pennsylvania and is Director of the Community and Minority Cancer Control Initiative at the Abramson Cancer Center. Dr. Hughes has conducted a significant amount of research on the contribution of sociocultural and psychological factors to cancer prevention and control. Her prior work includes research on ethnic differences in perceived risk of developing cancer, knowledge and attitudes about genetic testing for inherited cancer risk, and responses and preferences for education about genetic testing for inherited cancer risk. She was PI of an observational study funded by the Susan G. Komen National Race for the Cure Foundation to increase access to genetic counseling and testing among African American women. Dr. Hughes is currently PI of a randomized trial funded by the Department of Defense to develop and evaluate a culturally tailored genetic counseling protocol for African American women. She has published widely on ethnic differences in cancer prevention and control behaviors among African American women and has experience in developing and evaluating psycho-educational interventions targeted to breast cancer survivors through qualitative and quantitative methods.